safeMinds

Sensible Action For Ending Mercury-Induced Neurological Disorders

Date: March 7, 2007

Docket # 2006P-0535

The Coalition for SafeMinds supports the recommendation banning the use of mercury (thimerosal) in all prescription and over the counter products approved by the Food and Drug Administration. Below please find facts to support this request which include:

1. Adequate safety studies were not conducted prior to marketing thimerosal as a vaccine preservative.
2. Thimerosal's track record as a preservative documents toxicity and ineffectiveness.
3. Mercury exposure resulting from thimerosal-containing vaccine administration results in mercury levels where adverse outcomes are documented to occur.
4. Exposure to vaccine level thimerosal crosses the blood brain barrier and results in significant deposition of inorganic mercury in the brain.
5. U.S policy is falling behind other countries on this important health issue and is not in keeping with the Institute of Medicine's 2001 recommendations.
6. Not stating a preference for mercury-free vaccines reduces public confidence in the National Immunization Program.

1. **Adequate safety studies were not conducted prior to marketing thimerosal as a vaccine preservative**

As part of the Food and Drug Administration (FDA) Modernization Act, an assessment of thimerosal use in vaccines was conducted from 1997 to 1999. The FDA investigation was unable to locate any clinical studies formally evaluating the use of thimerosal before its initial marketing in the 1930's.[2] The only study found was from 1931 where thimerosal was administered to individuals suffering from meningitis. The study was not designed to specifically examine toxicity; no clinical assessments were described nor were laboratory studies reported. "Merthiolate was injected intravenously into 22 persons…these large doses did not produce any anaphylactoid or shock symptoms." In the paper, the authors acknowledge the clinician who treated the meningitis patients was not convinced of its efficacy stating "beneficial effects of the drug were not definitely proven." Industry scientists noted in 1930 that a "wide range of toxicity and injury tests should be done."[3] There is no evidence that the scientists took their own advice and conducted studies to address these concerns. According to FDA's own investigation, vaccine manufacturers were not required to evaluate thimerosal's safety in animal studies prior to its introduction as a preservative in vaccines although federal regulations require formal submission of animal safety data for finished biological products, including active and inactive ingredients. [4]

Therefore, the FDA never required the pharmaceutical industry to conduct extensive toxicological testing, the bedrock of pharmaceutical development, on thimerosal necessary to prove thimerosal was safe before it went on the market. They failed to require industry to conduct adequate testing to determine how thimerosal is metabolized and they failed to require that industry conduct studies to determine the maximum safe exposure level of thimerosal. Furthermore, adequate safety testing has not been done to this day.

2. Thimerosal's track record as a preservative documents toxicity and ineffectiveness

Despite the fact that there were never proper studies done to evaluate the potential toxicity of thimerosal prior to marketing, there is ample evidence provided by federal agencies and independent scientists that spans the last 70 years which documents that thimerosal is not an effective or safe vaccine preservative. In a study published in the *Journal of the American Medical Association* in 1948 titled "The bacteriostatic and bactericidal actions of some mercurial compounds on hemolytic streptococci," the authors vigorously argued that thimerosal was ineffective as a "disinfectant, germicide and antiseptic." In the review of the literature in this paper, the authors cited eight studies from 1928, 1935, 1937, 1938, and 1944 all of which drew similar conclusions.[5]

In 1975, the FDA convened a panel of experts which included the lead author of the 1948 paper cited above to evaluate mercury-containing over-the-counter (OTC) products. The panel issued its reports in 1980 and in 1982. The FDA issued a report of the panel's findings in the Federal Register where they concluded that "some mercury-containing preparations are not effective and others are not safe and effective for OTC topical antimicrobial use. [6] A bacteriostatic action that is capable of being reversed by contact with body fluids and other organic matter does not constitute an effective topical antimicrobial action…" Most of the literature reviewed addressed mercury's lack of antibacterial properties. One study reviewed published in 1970 titled, "Three thousand years of mercury. A plea for abandonment of a dangerous, unproven therapy," addressed mercury's lack of effectiveness regarding anti-fungal properties. [7]

With respect to thimerosal in particular, the panel found evidence from 1950 which concluded that "thimerosal was no better than water in protecting mice from potential fatal streptococcal infections."[8] Additionally, citing a 1935 study, the panel reported that thimerosal was "35.3 times more toxic for embryonic chick heart tissue than for

Staphylococcus aureus."[9] The panel concluded that "thimerosal was not safe for OTC topical use because of its potential for cell damage if applied to broken skin and its allergy potential. It is not effective as a topical antimicrobial because its bacteriostatic

action can be reversed." However, it wasn't until 1998 that the FDA issued its final report banning the use of thimerosal in topical OTC products because they were not "safe and effective."[10]

There are several recent reports of thimerosal's failure as a preservative. Clusters of disease from *Group A streptococcus* infections were traced back to multi-dose vials of diphtheria toxoid, pertussis, and tetanus toxoid (DPT) vaccine which were contaminated after being opened. [11] Additionally, in 2004, a Chiron plant that manufactured Fluvirin was forced to close because its vaccine was contaminated with *Serratia marcescens*.[12] This vaccine used thimerosal as a preservative in its product. This plant closure created shortages in the vaccine supply and caused concern among providers and patients. In this case and others, thimerosal failed to prevent bacterial growth.

3. **Mercury exposure resulting from thimerosal containing vaccine administration results in mercury levels where adverse outcomes are documented to occur.**

A 2002 study reported a mercury blood level in a 2-month-old infant of 20.55 nmol/L five days after the infant received a 37.5 µg dose of ethylmercury (the amount contained in one DTaP and one Hepatitis B vaccine). [13] Many infants, however, beginning in the early 1990's and for the next decade, received a 62.5 µg dose of ethylmercury (adding in the Haemophilus influenzae type b (Hib) vaccine) at the 2-month well baby visit. A vaccine expert from the Johns Hopkins Institute for Vaccine Safety estimated that these infants may have experienced peak blood mercury levels of 48.3 nmol/L;[14] well above the presumed EPA safety threshold of 29.0 nmol/L. As a reference point, the CDC recently defined a toxic exposure to mercury in an adult as a blood mercury level of >10µg /L (50 nmol/L) -- approximately the same blood level that some infants experienced at two months of age.[15]

Additionally, a study published in Pediatrics in 2000 measured blood mercury levels in newborns administered the Hepatitis B vaccine, containing 12.5 µg ethyl mercury. The investigation documented elevated post-immunization concentrations relative to pre-immunization levels in all neonates studied. [16] Levels of blood mercury after exposure in low birth weight infants were 7.36 (± 4.99) µg/L. One infant was found to have developed a mercury level of 23.6 µg/L, thus meeting the CDC criteria as a case of chemical poisoning from mercury.

Experts contend that there are "windows of vulnerability" which occur during neurological development and that specific types of developmental outcomes may have separate windows of vulnerability. [17] These critical periods of development have not been established and may be relatively short in duration. The fact that thimerosal from vaccines has been documented to raise blood mercury levels concentrations over known

thresholds where developmental effects have been documented to occur during the first few months of life means that particular "windows of vulnerability" may have been breeched. Even minor neurological impairment can have profound societal effects when amortized across the entire population and life span.[18]

In addition, EPA recently revised an earlier report which doubled the estimate of the number of newborn children at risk for developing adverse neurological outcomes due to elevated mercury levels. This revision was in response to finding that mercury cord blood levels were approximately 70% higher than maternal levels at the time of delivery. These new findings estimate that 1 in every 6 infants is already at risk for neurological injury from mercury.[19] Adding additional mercury exposure from thimerosal only serves to further increase the risk of injury.

4. **Exposure to vaccine level thimerosal crosses the blood brain barrier and results in significant deposition of mercury in the brain**.

A 2005 study funded by the National Institutes of Health compared brain mercury levels in infant Macaca fascicularis primates exposed to: 1) injected ethylmercury (thimerosal) and 2) equal amounts of ingested methylmercury.[20] In this study, ethylmercury more rapidly converted to inorganic mercury in the brains of the primates which resulted in increasing levels of inorganic mercury. In fact, the primates exposed to ethylmercury retained at least twice as much inorganic mercury in their brains compared to the primates exposed to methylmercury. Specifically, the relative concentrations in monkeys with detectable levels of inorganic mercury were 16 ng/g in thimerosal-treated monkeys and 7 ng/g in the methylmercury-treated monkeys in which inorganic mercury levels were detectable. Inorganic mercury was below detectable levels in 8 out of 17 of the methylmercury-treated monkeys. Exposures to mercury during these critical periods of development disrupt the growth and migration of neurons, with the potential to cause irreversible damage to the central nervous system.

Prior research into the effects of methylmercury in adult primates documents that inorganic mercury in the brain is deposited in microglial and astroglial cells more than other cells and that inorganic mercury becomes trapped in the brain, the estimated half-life is over 700 days and that inorganic mercury is the toxic agent responsible for pathological changes in microglial and astroglial cells.[21] Chronic microglial activation has been recognized as an important component of neuro-degenerative disease and neuro-inflammation and contributes to neuronal dysfunction and injury.[22] Microglial cells serve as the brain's immune system, and chronic activation of this system leads to pathological consequences, specifically, neuro-inflammation. Autopsied brain tissue from autistic patients contains evidence of an active neuro-inflammatory process in the

cerebral cortex, white matter and the cerebellum as well as marked activation of microglial and astroglial cells. [23]

5. **U.S. policy is falling behind on this important health issue**

In the 1980's, several Russian articles were published investigating the toxicity of medical and biological preparations including vaccines. Specifically, in 1983 Kravchenko concluded that the methods of quality control, including tests on animals, do not ensure the complete absence of toxicity in a final product and that the use of the "subcultures with the introduced preparation" makes it possible to determine the toxicity of both specific and nonspecific components of vaccines and sera from the number of dead and damaged cells. The toxic action of preparations kills and damages the cells at the site of injection, thus inducing the formation of autoantigens whose effect on the body can not be predicted. Thus "thimerosal, commonly used as preservative, has been found not only to render its primary toxic effect, but also capable of changing the properties of cells. This fact suggests that the use of thimerosal for the preservation of medical biological preparations, especially those intended for children, is inadmissible."[24]

In another Russian paper, merthiolate (thimerosal) in a concentration of 1:10,000, contained in one dose of vaccine, was found to damage cells in subsequent 2-fold dilutions up to 1:128. It was found that all of the tested medical and biological preparations (MBP) containing this preservative have in common the ability to damage cells in titers up to 1:128. In contrast, anti-rabies and anti-influenza vaccines with no preservatives were found not to exhibit damaging or cytotoxic effects in titers not exceeding 1:2-1:4. They concluded that "merthiolate usage (thimerosal) for MBP preservation should be discontinued due to its high toxicity."[25]

In 1986, after performing an extensive survey of the literature on organic mercury compounds and their toxicity, a medical officer from the U.K.'s Department of Health and Social Security, remarked (in reference to the presence of thimerosal in multidose vaccines): "... it is now accepted that multidose injection preparations are undesirable and preservatives should not be present in unit-dose preparations."[26] This review concluded with the recommendation that consideration should be given to replacing organic mercurial preservatives in medicinal products.

Others have raised concerns about vaccinating pregnant women with thimerosal-containing products and vaccines including influenza. Specifically, in a 2001 article titled "Vaccines without thimerosal: why so necessary, why so long coming?" the author states that although very low concentrations of thimerosal in pharmacologic and biological products are relatively non-toxic, this is probably not the case for in utero

exposures or those occurring during the first six months of life.[27] Additionally, a Dutch report cautioned that thimerosal-containing immunoglobulins should not be administered to pregnant travelers because exposure to ethylmercury may cause harm to the fetus.[28] Vaccines containing thimerosal were previously phased out in Denmark and Sweden. Just last year the UK announced a ban on thimerosal containing vaccines, "Mercury will be banned from vaccines given to babies, the Department of Health said last night amid fears of links between the metal and autism." [29]

6. **Not banning mercury from vaccines reduces public confidence in the FDA**

According to a recent study conducted by the University of Michigan, vaccine safety concerns have increased among both parents and physicians.[30] In cooperation with the CDC, the researchers surveyed nearly 750 randomly selected pediatricians and family practitioners across the United States. They found that nearly 70 percent of doctors said that parent worries have risen recently, and more than a third of the physicians reported their own concerns had also increased with regard to safety issues. Additionally, the increase in concern resulted in a decrease in vaccine uptake. More than 90 percent of pediatricians and 60 percent of family practitioners reported that at least one parent had refused to allow their child to receive a particular vaccine in the past year. And up to a third of family physicians and 12 percent of pediatricians said they did not recommend particular vaccines to parents either routinely or occasionally. Many of the doctors themselves said the rotavirus and thimerosal issues had increased their own concern about vaccine safety, as well as that of parents.

In an effort to understand why parents and physicians alike are concerned about thimerosal it is important to understand just how much mercury is in vaccines preserved with thimerosal. Thimerosal is typically added to vaccines at a concentration of 1:10,000 which is equivalent to 100,000 parts per billion (ppb). Because thimerosal is almost one-half mercury, the concentration of mercury in the vaccine vial is at 50,000 ppb. To put this in perspective, the EPA requires liquid waste which exceeds 200 ppb of mercury to be sent to a special hazardous waste landfill and according to the EPA, drinking water cannot exceed 2 ppb of mercury. Therefore, unused thimerosal-preserved vaccines must be disposed of as a hazardous waste.

In summary, the introduction of thimerosal into vaccines appears to have been based on a single, uncontrolled and poorly reported human study in the late 1920s. However, this sole human study was not a true safety study and produced a faulty foundation upon which to build a robust vaccine program in which infants would receive multiple doses of ethylmercury. Even today, 70 years after the introduction of thimerosal into infant vaccines we still do not have adequate safety data with regard to the toxicity of thimerosal to support its continued use in vaccines. As a preservative, thimerosal's track record is dubious at best due to several episodes of contamination in addition to its

known toxic properties. Levels of mercury documented in infants after exposure to thimerosal-containing vaccines have reached levels classified by the CDC as mercury chemical poisoning. These same exposure levels in infant primates resulted in significant deposition of inorganic mercury in the brain. The recent recommendation that infants, in addition to pregnant mothers, receive flu vaccine results in children receiving 53% of the amount of mercury received in 1999 when the initial recommendation was made to decrease exposure due to potential health concerns. By not banning thimerosal the FDA is not keeping current with international practices and is putting in jeopardy the entire US vaccine program. In light of these facts, is it reasonable to expect consumers to feel confident that thimerosal-containing vaccines are safe and then readily accept them? The use of such a toxic substance when its efficacy is doubtful, its safety not documented, and its use results in brain accumulation of mercury is difficult to justify, especially when less hazardous and more effective substances exist that can be used to preserve vaccines.

Respectfully submitted,

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